REMARKS

Claims 1-41, 50-57, 74-82 and 102-116 were pending in this application. Claims 39-41, 50-57 and 74-82 were withdrawn from consideration. Claims 1-38 and 102-116 were under consideration at the time of the most recent office action. Claims 2, 4, 13, 25, and 34 are now canceled without prejudice such that claims 1, 3, 5-12, 14-24, 26-33, 35-38, and 102-116 are now currently under review. All amendments have been made without prejudice.

Specification/Priority

The specification has been amended to address an informality noted by the Examiner. The specification has been amended to indicate that the current application is a continuing application.

Claim Rejections under 35 U.S.C. § 112

A. Claims 1-38 and 102-116 stand rejected under 35 U.S.C. §112, second paragraph, as indefinite for allegedly failing to particularly point out and distinctly claim the subject matter which Applicants regard as their invention.

The Examiner has alleged that in claim 1 (and in dependent claims therefrom), the term "modified alpha amino acid residue" lacks metes and bounds as to the modifications and resulting structure encompassed by the claimed invention. Applicants have amended claim 1 to simplify its form and to focus upon certain preferred embodiments. In so doing, the phrase objected to by the Examiner has been removed. Claim 1 now recites an "α-amino acid residue." Persons of skill in the art will appreciate the breadth of this element in the context of the present invention and in particular that naturally occurring alpha amino acids, and modified alpha amino acids are each a kind of "α-amino acid residue."

B. Claims 1, 2, 102 and 103 (and dependent claims therefrom) are alleged to be indefinite for the recitation of the term "disaccharide modified to bear" with regard to "what chemical portion of the saccharide is being modified and . . . which sugar residue(s) are being modified." In claim 1, it will be clear to one of skill in the art the glucose residue linked directly to the group A_4 is the glucose group being modified. Claim 2 has been canceled. In claims 102 and 103, which refer to a first and second saccharide group, the language is

believed to clarify that the second saccharide group directly attached to the glycopeptide is the sacchride group being modified.

C. Claim 1 is alleged to be incomplete for the omission of essential structural cooperative relationships of elements recited therein. The Office Action alleges, at page 7, that the unclaimed essential matter is the location of "the 'glycosidic bond' . . . formed between the peptide and glycosyl group(s) to form the glycopeptide." While it is true that traditional vancomycin antibiotic nomenclature is awkward, here all "essential cooperative relationships of elements" have been provided. Claim 1 recites that "the group A_4 is linked via a glycosidic bond to a disaccharide." Skilled artisans understand where and how glycosidic linkages can be formed between the group A_4 of the peptide and the disaccharide. The same is not indefinite.

D. Claim 1 is urged to be indefinite with regards to the upper limit of how many glycosidic groups may be linked to one or more of the groups A_1 through A_7, how many sugar residues a glycosidic group may contain, and what that structure would be. This rejection is addressed by the present amendment.

E. Claims 102 and 107 are said to be indefinite, as lacking metes and bounds to the encompassed substituents and ultimate structure of a "substituted amino group." The skilled artisan knows the kinds of substituents that may be attached to the amino group of an aminosaccharide residue in the claimed glycopeptides. Many examples of such substituents are disclosed throughout the specification and the applicability of this invention to a variety of substitutions is one of the advantages of the invention. One of skill in the art would clearly understand the metes and bounds of a "substituted amino group" in the context of the claimed invention.

F. Claim 102 is said to be indefinite for the recitation of the phrase "modified to bear at least one substituent which is not hydroxyl" with respect to the encompassed substituents. In an effort to provide improved clarity and organization to the claims, claim 102 has been amended to recite "[a] glycopeptide antibiotic bearing at least one disaccharide group, said disaccharide group comprising two saccharide groups, a first of said saccharide groups bearing at least one amino or substituted amino group, and a second of said saccharide groups linked directly to said glycopeptide is modified to bear at least one substituent of the formula of the formula YXR, $N^+(R_1)=CR_2R_3$, $N=PR_1R_2R_3$, $N^+R_1R_2R_3$ or $P^+R_1R_2R_3$, in which

the group Y is a single bond, O, NR_1 or S; the group X is O, NR_1, S, SO_2, C(O)O, C(O)S, C(S)O, C(S)S, $C(NR_1)O$, $C(O)NR_1$, or halo (in which case Y and R are absent); and R, R_1, R_2, and R_3 are independently hydrogen, alkyl, aryl, aralkyl, alkanoyl, aroyl, aralkanoyl, heterocyclic, heterocyclic-carbonyl, heterocyclic-alkyl, heterocyclic-alkyl-carbonyl, alkylsulfonyl or arylsulfonyl, provided that the substituents of the formula YXR is not hydroxyl; X and Y are not both O; X and Y are not S and O, or O and S, respectively; and if two or more of said substituents are present, they can be the same or different". One skilled in the art will recognize what substituents may be attached to the saccharide, which are contemplated by the invention. While this nomenclature is complex, it is necessarily so. It is not, however, unclear or indefinite.

Rejections under 35 U.S.C. §112, first paragraph

Claims 1 – 38 and 102 – 116 have been rejected under 35 U.S.C. §112, second paragraph for alleged lack of enablement. It is alleged, at page 5 of the Official Action, that "the specification, while being enabled for vancomycin glucose C6 substituted derivatives of original claim 83-101, ... the specification does not reasonably provide enablement for the full scope of glycopeptides or glycopeptide antibiotics of claims 1 and 102 (and claims dependent thereon)." Applicants respectfully traverse this rejection. The present amendment focuses (without prejudice) to certain preferred embodiments. The pending claims are both as clear as the complex technology permits and fully enabled.

Whenever the adequacy of enablement provided by an Applicant's specification is challenged, the Examiner has the initial burden of giving reasons, supported by the record as a whole, why the specification is not enabling. The enablement requirement is satisfied if a disclosure contains sufficient information such that persons of ordinary skill in the art, having the disclosure before them, would be able to make and use the invention. The legal standard for enablement under §112 is whether one skilled in the art would be able to practice the invention without undue experimentation. *In re Wands*, 8 U.S.P.Q.2d 1400 (Fed. Cir. 1988).

As an initial matter, the Examiner is asked to acknowledge the very large number of actual, working examples presented in the application. These are illustrative of the breadth of the invention and are supportive of its enablement. The invention is broad by nature and

must be seen to be so. Whatever experimentation may be required is greatly abbreviated by the extensive teachings of the specification. Experimentation is not undue so long as it is of a routine nature. *Ex parte Forman*, 230 U.S.P.Q. 546, 547 (Pat. Off. Bd. App. 1986).

> The test [for undue experimentation] is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the claimed invention.

PPG Indus., Inc. v. Guardian Indus. Corp., 37 U.S.P.Q.2d 1618, 1623 (Fed. Cir. 1996) (quotation and citation omitted).

With regard to the enablement determination, the following statement from *In re Marzocchi*, 169 U.S.P.Q. 367, 369-370 (C.C.P.A. 1971), is noteworthy:

> The only relevant concern of the Patent Office under these circumstances should be over the truth of any such assertion. The first paragraph of §112 requires nothing more than objective enablement. How such a teaching is set forth, either by the use of illustrative examples or by broad terminology, is of no importance.
>
> As a matter of Patent Office practice, then, a specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as in compliance with the enabling requirements of the first paragraph of §112 unless there is reason to doubt the objective truth of the statements contained therein which must be relied upon for enabling support.

The law thus requires that the Patent Office accept Applicants' assertion of enablement or provide reasoning and evidence to substantiate doubts of the objective truth of Applicants' assertion. *In re Dinh-Nguyen*, 181 U.S.P.Q. 46 (C.C.P.A. 1974); *In re Bowen*,

181 U.S.P.Q. 48 (C.C.P.A. 1974). Given the present claim focus on certain preferred embodiments together with the extensive exemplification of the specification, it is strongly submitted that enablement has been shown and that the requirements of the first paragraph of 35 U.S.C. §112 have been met. Moreover, the arguments and amendments detailed above in response to the Examiner's contention that the claims were indefinite likewise obviate the present enablement rejections. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 1, 3, 5-12, 14-24, 26-33, 35-38, and 102-116 under 35 U.S.C. §112, first paragraph.

Claim Rejections under 35 U.S.C. § 102

A. Claims 1, 102 and 103 are rejected under 35 U.S.C. §102(a) or (b) as allegedly being anticipated by Stack *et al.* EP 0802199A2 ("Stack"). Applicants traverse. The standard for anticipation under §102(a) and (b) is one of strict identity. An anticipation rejection requires a showing that each limitation of a claim be found in a single reference. *Atlas Powder Co. v. E.I. DuPont de Nemours & Co.*, 224 U.S.P.Q. 409, 411 (Fed. Cir. 1984).

Stack fails to teach every limitation of Applicants' invention. Claim 1 is directed to "a glycopeptide of the formula A_1-A_2-A_3-A_4-A_5-A_6-A_7... wherein the group A_4 is linked via a glycosidic bond to a disaccharide having a glucose residue directly attached to said A_4 residue, wherein said glucose residue bears an N-substituted aminohexose residue, and at least one substituent of the formula YXR, $N^+(R_1)$=CR_2R_3, N=$PR_1R_2R_3$, $N^+R_1R_2R_3$ or $P^+R_1R_2R_3$...". Stack does not teach a glycopeptide containing a substituted disaccharide attached at the A_4 position of the peptide, *wherein the saccharide group directly attached to the group A_4 is modified.* Therefore, Stack does not anticipate Applicants invention.

Claim 102 (and dependent claim 103) is directed to "a glycopeptide antibiotic bearing at least one disaccharide group, said disaccharide group comprising two saccharide groups, ... and a second of said saccharide groups linked directly to said glycopeptide is modified to bear at least one substituent of the formula YXR, $N^+(R_1)$=CR_2R_3, N=$PR_1R_2R_3$, $N^+R_1R_2R_3$ or $P^+R_1R_2R_3$, in which the group Y is a single bond, O, NR_1 or S; the group X is O, NR_1, S, SO_2, C(O)O, C(O)S, C(S)O, C(S)S, C(NR_1)O, C(O)NR_1, or halo (in which case Y and R are absent); and R, R_1, R_2, and R_3 are independently hydrogen, alkyl, aryl, aralkyl, alkanoyl, aroyl, aralkanoyl, heterocyclic, heterocyclic-carbonyl, heterocyclic-alkyl, heterocyclic-alkyl-

carbonyl, alkylsulfonyl or arylsulfonyl, provided that the substituents of the formula YXR is not hydroxyl; X and Y are not both O; X and Y are not S and O, or O and S, respectively; and if two or more of said substituents are present, they can be the same or different…". As stated above, Stack fails to teach a glycopeptide antibiotic containing a substituted disaccharide, *wherein the saccharide group directly attached to the peptide is modified.* Since Stack fails to anticipate Applicants' invention, this rejection should be withdrawn.

B. Claims 1, 102 and 103 are rejected under 35 U.S.C. §102(e) as allegedly being anticipated by Cooper *et al.*, U.S. Pat. No. 5,843,889 ("Cooper"). Applicants traverse.

Claim 1 is directed to "a glycopeptide of the formula A_1-A_2-A_3-A_4-A_5-A_6-A_7… wherein the group A_4 is linked via a glycosidic bond to a disaccharide having a glucose residue directly attached to said A_4 residue, wherein said glucose residue bears an N-substituted aminohexose residue, and at least one substituent of the formula YXR, $N^+(R_1)=CR_2R_3$, $N=PR_1R_2R_3$, $N^+R_1R_2R_3$ or $P^+R_1R_2R_3$…". Cooper does not teach a glycopeptide containing a substituted disaccharide attached at the A_4 position of the peptide, *wherein the saccharide group directly attached to the group A_4 is modified.* Therefore, Cooper does not anticipate Applicants invention.

Claim 102 (and dependent claim 103) is directed to "a glycopeptide antibiotic bearing at least one disaccharide group, said disaccharide group comprising two saccharide groups, … and a second of said saccharide groups linked directly to said glycopeptide is modified to bear at least one substituent of the formula YXR, $N^+(R_1)=CR_2R_3$, $N=PR_1R_2R_3$, $N^+R_1R_2R_3$ or $P^+R_1R_2R_3$, in which the group Y is a single bond, O, NR_1 or S; the group X is O, NR_1, S, SO_2, C(O)O, C(O)S, C(S)O, C(S)S, $C(NR_1)O$, $C(O)NR_1$, or halo (in which case Y and R are absent); and R, R_1, R_2, and R_3 are independently hydrogen, alkyl, aryl, aralkyl, alkanoyl, aroyl, aralkanoyl, heterocyclic, heterocyclic-carbonyl, heterocyclic-alkyl, heterocyclic-alkyl-carbonyl, alkylsulfonyl or arylsulfonyl, provided that the substituents of the formula YXR is not hydroxyl; X and Y are not both O; X and Y are not S and O, or O and S, respectively; and if two or more of said substituents are present, they can be the same or different…". As stated above, Cooper fails to teach a glycopeptide antibiotic containing a substituted disaccharide, *wherein the saccharide group directly attached to the peptide is modified.* Since Cooper does not anticipate Applicants' invention, this rejection should be withdrawn.

C. Claims 1-6, 9-15, 18-27 and 30-38 stand rejected under 35 U.S.C. §102(e) as allegedly being anticipated by Ge et al., Science col. 284 (publication date of April 16, 1999) ("Ge"). Applicants respectfully traverse.

First, Applicants submit that Ge is an improper §102(e) reference, since §102(e) references are limited to "patents and patent applications" and Ge is neither Applicants presume that the Examiner intended to assert Ge as a §102(a) or (b) reference against claims 1-6, 9-15, 18-27 and 30-38. In that case, applicants submit that Ge is also an improper §102(a) or (b) reference. The present invention claim priority to U.S. Patent Application No. 09/353,368, filed July 14, 1999, which in turn claims benefit of Provisional Application Serial No. 60/134,839 filed May 19, 1999, as well as benefit of U.S. Patent Application No. 09/115,667, filed July 14, 1998 (since converted to Provisional Application No, 60/150,690). Ge was available as §102(a) or (b) reference as of its publication date of April 16, 1999. Since Applicants have perfected a priority claim to July 14, 1998, Ge is not a proper §102(a) or (b) reference and Applicants request that the rejection over Ge be withdrawn.

D. Claims 1-38 and 102-116 stand rejected under 35 U.S.C. 102(e) as being anticipated, or alternatively rendered obvious, over Kahne, WO 00/42067 ("Kahne"). Applicants traverse this rejection.

Applicants submit that Kahne is an improper §102(e) reference. Kahne has an international filing date of January 12, 2000, which is before November 29, 2000, and therefore, the pre-AIPA amendment version of §102(e) applies to Kahne in determining the date Kahne is available as a prior art reference. The pre-AIPA version of 35 U.S.C. §102(e) states:

> A person shall be entitled to a patent unless-
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Publications of international applications filed before November 29, 2000 do not have a 35 U.S.C. §102(e) date at all, and therefore Kahne is not a proper 102(e) reference. See M.P.E.P. 706.2 (a). Furthermore, although publications of international applications filed

before November 29, 2000 are available as prior art under 35 U.S.C. §102(a) or (b) as of their publication date, Kahne is not a proper §102(a) or (b) reference since its international publication date is July 20, 2000, which is after Applicants' earliest filing date of July 14, 1998. Therefore, rejection over Kahne is improper and should be withdrawn.

Double Patenting Rejections

A. Claims 1-38 and 102-116 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-47 of U.S. Patent No. 6,498,238 ("the 238 patent"), over claims 1-19 of U.S. Patent No. 6,841,661 ("the 661 patent"), and over claims 1-19 of U.S. Patent No.6,710,168 ("the 168 patent").

Pursuant to 37 C.F.R. §1.78(c) and 35 U.S.C. §132, the assignee confirms that the present application, the 238 patent, and the 661 patent were commonly owned by the assignee at the time the invention of the present application was made.

Applicants respectfully traverse the double patenting rejections. Given the present claim focus on certain preferred embodiments, together with the extensive exemplification of the specification, it is submitted that the present claims are not rendered obvious in view of the issued claims of the 238, 661 or 168 patents. Therefore, Applicants request that the Examiner reconsider and withdraw these rejections.

Conclusion

Applicants submit that claims 1, 3, 5-12, 14-24, 26-33, 35-38, and 102-116 are in condition for allowance. A notice of allowance is earnestly solicited. If the Examiner feels a telephonic interview would be helpful, he is asked to call the undersigned at the telephone number below.

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